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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,933	CAO ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-76* is/are pending in the application.

4a) Of the above claim(s) *42-45,48-53,56-59,69-72,75 and 76* is/are withdrawn from consideration.

5)☒ Claim(s) *35 and 37* is/are allowed.

6)☒ Claim(s) *30-34,36,38-41,46,47,54,55,60-68,73 and 74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 30-76 are pending in the application.

2. Because this action raises new grounds of rejection, it is made Non-Final.

Election/Restrictions

3. Applicant's election with traverse of Group I in the reply filed on July 11, 2006 is acknowledged. The traversal is on the ground(s) that the various inventions are drawn to similar subject matter (related inventions) and that there would be economic hardship on the Applicant if the Requirement for Restriction was to be maintained. These arguments are not found persuasive. With respect to the first argument, that the various inventions are drawn to similar subject matter, such was acknowledged in the Requirement for Restriction. However, as was also indicated in the Restriction Requirement, while the inventions are related, they nonetheless represent distinct inventions. This argument is therefore not found persuasive.

The second argument is also not found persuasive, as there is also hardship on the Office in having to search and examine multiple inventions in a single application.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 42-45, 48-53, 56-59, 69-72, 75, and 76 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 11, 2006.

5. Claims 30-41, 46, 47, 54, 55, 60-68, 73, and 74 are under consideration.

Specification

6. **(New Objection)** The amendments filed March 1, 2005 and February 22, 2006 are objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the amendment of the application to incorporate the subject matter of U.S. Patents 6,168,942; 6,410,032; and 6,410,299. The Applicant submitted these amendments to refer to these patents as a correction for the indicated typographical error referring to a prior patent application 08/107,908. The amendment was made on the basis that the patents included the subject matter that was intended to be incorporated by reference, which material is found in provisional application number **60**/107,908. See, Response of March 1, 2005.

It is noted that where there has been an improper incorporation by reference, an applicant may correct such where the proper reference "is sufficiently described to uniquely identify the document." See, MPEP 608.01(p) I.A.2. In the present case, there is no such unique identification of the provisional application 60/107,908. This is because the application originally referred to the wrong application. While it would have been apparent to those in the art that the 08/108,908 application was not the correct application once it had been reviewed, those in the art would not have known what application was intended by the present Application. Because there is insufficient identification of the 60/107,908 application, this is also insufficient support for the amendment referring to the indicated patents, which claim priority thereto. The

amendment referring to these patents, and incorporating the subject matter therein by reference is therefore New Matter to the application.

Applicant is required to cancel the new matter in the reply to this Office Action.

7. **(New Objection)** The disclosure is objected to because of the following informalities: the most recent amendment to the specification (submitted on February 2, 2006 does not comply with the requirements of 37 CFR 1.121. The amendment does not show the changes made to the application relative to the immediately prior version of the specification. The amendment of 2/22/06 shows amendments to paragraphs on pages 2, 5, 13, and 15; showing the changes relative to the pargraphs as submitted in the application as filed. However, the paragraphs of pages 2 and 5 had been previously amended on March 1, 2005, and the paragraphs on pages 13 and 15 had been amended on October 10, 2005. Thus, the amended paragraphs represent the immediately prior versions of the paragraphs according to 37 CFR 1.121(b). See MPEP 714 II. B. Because the amendment of 2/22/06 shows the changes relative to the originally filed application, and not the immediately prior version of the application, the amendment is considered non-compliant .

Applicant is required to present a new version of the amendment showing the changes relative to the immediately prior versions of the indicated paragraphs.

Claim Objections

8. **(Prior Objection- Withdrawn)** Claims 32, 34, 38, 43, 45, and 49 are objected to because the claims lack periods. In view of the amendment to the claims, the objection is withdrawn.

9. **(New Objection)** Claims 30 and 31 are objected to because of the following informalities: Claim 30 is treated as representative. This claim reads on a virus comprising in its genome an intact 5' region of "at lease 36 base pairs." The term "lease" appears to be a typo for - - least- -. Appropriate correction is required.

Claim Rejections - 35 USC § 101

10. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. **(New Rejection)** Claims 39, 40, 63, and 64 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. These claims are drawn to cells transformed with a vector. Because the claims are drawn to cells, and not to isolated cells, the claims read on human beings. Thus, the claims read on non-statutory subject matter.

It is suggested that the claims be amended to read on - - isolated cells- -.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. **(Prior Rejection- Withdrawn)** Claims 30, 32-34, 36 and 38-59 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30, 32-34, and 42-45 recited the phrase "at least about." It was not clear what is intended by this phrase. In view of the cancellation of this language, this ground of rejection is withdrawn.

Claims 30, 32-34 and 42-45 were also rejected because it cannot be determined from the language recited how Npro is mutated since "at least" 36 or 310 base pairs of the 5' region remains intact. Applicant's arguments are found persuasive; the indefinitness rejection is therefore withdrawn.

Claims 36 and 38-41 were rejected as lacking antecedent basis regarding its dependency from claim 37. In view of the amendments to the claims, the rejection is withdrawn.

Claims 38, 40, 47, 49, 51, 52, 55, and 57 were rejected for lack of antecedent basis with respect to dependency from claims 36 and 37. In view of the amendments to the claims, the rejection is withdrawn.

14. **(New Rejection)** Claim 31, 60-68, 73, and 74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims are rejected on two grounds.

For the first ground, claim 31 is treated as representative. This claim is drawn to an attenuated BVDV comprising a genomic sequence as set forth in SEQ ID NO: 11, wherein the

virus comprises a mutated N^{pro} sequence of at least 36 base pairs. SEQ ID NO: 11 is disclosed in the application as an attenuated BVDV genome comprising 308 (504-196) base pairs. It is not clear from the claims if the claims are intended to be directed to the attenuated virus of SEQ ID NO: 11 (BVDVN6- disclosed on page 7), or on any attenuated BVDV virus comprising a genome with up to the 308 base pairs of the N^{pro} sequence present in SEQ ID NO: 11.

For the second ground, claim 60 is treated as representative. This claim is directed to the virus of claim 31, wherein the N^{pro} sequence comprises an intact 5' region of at least 310 base pairs. Because only 308 base pairs are present in the N^{pro} sequence of claim 31, it is not clear how claim 60 can limit the N^{pro} sequence therein to embodiments comprising more than 308 base pairs. It is therefore not clear what the scope of claims 60-68 is.

Because it appears that the Applicant intends the language of the claims to include embodiments wherein the viral genome includes N^{pro} sequences in addition to the 308 base pairs provided in the claim 11, the claims are read as including any BVDV N^{pro} sequence comprising any mutated N^{pro} sequence including a mutated full-length N^{pro} sequence. As is indicated on page 7 of the application, such mutations include any insertion, deletion, or substitution in the N^{pro} sequence such that the N^{pro} protein is inactivated.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. **(New Rejection)** Claims 30-34, 36, 38-41, 46, 47, 54, 55, 60-68, 73, 74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description

requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims read on a genus of attenuated bovine viral diarrhea viruses, the viruses comprising a mutated N^{pro} coding sequence comprising an intact 5' region of at least 36 (or 310) base pairs, wherein the mutated N^{pro} coding sequence encodes an inactive N^{pro} protein.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed.

In the present case, the Applicant has provided only one species of the claimed invention- the mutated genomic sequence of SEQ ID NO: 11, in which the N^{pro} sequence is truncated at nucleotide 308 (504-196). See, page 7. Contrary to Applicant's assertion on page 12 of the Response, the claims do read on intact N^{pro} sequence, so long as the intact sequence includes an

inactivating mutation (including any insertion, deletion, or substitution that inactivates the N^{pro} protein). App., page 7 (lines 1-8). Moreover, while the application indicates that the mutated N^{pro} sequences require that the N^{pro} protein is inactivated (thereby providing a functional identifying characteristic); the application does not provide sufficient structural (or other non-functional) identification of the claimed N^{pro} sequence mutations to demonstrate possession of the full scope of the claimed genus.

In particular, while the application indicates that deletion of the 196 3' base pairs resulted in an inactive N^{pro} protein, the application does not identify what other regions within the N^{pro} sequence would similarly result in such inactivation. Nor does the application identify what residues within the N^{pro} protein are required for the protein's activity such that those in art would know which residues or structures in the protein to target for modification to inactivate the protein through other mutations than deletion of at least 196 base pairs from the 3' end of the N^{pro} gene sequence.

In addition to the limited guidance as to what specific regions of amino acid coding sequences may be modified to result in the loss of N^{pro} activity, the art indicates that there is significant uncertainty in the art of protein modification. See e.g., Bowie et al., Science 247: 1306-10. In particular, the Bowie reference indicates that the effects of amino acid modifications made to protein sequences are unpredictable absent specific teachings as to the relationship between the amino acid(s) to be modified and the overall structure and function of the protein. Id. In the present case, there is no identification of any specific region or amino acid residues in the N^{pro} protein that are indicative of the protein's activity.

It is further noted that the Applicant has asserted, with respect to the enablement rejection presented in the prior action, that "those skilled in the art may conduct additional experimentation in order to inactivate the N^{pro} gene and screen for mutations according to the invention." Thus, the Applicant has indicated that such additional screening would be required in order for those in the art to determine what modifications correspond to the required function. Moreover, it is additionally noted that the provision of methods to identify compounds with a particular function is not sufficient to demonstrate possession of the compounds that may be identified using such methods. See e.g., *University of Rochester v. G.D. Searle & Co.*, 69 U.S.P.Q.2d 1886, at 1895 (CAFC 2004). Thus, the existence of such methods fails to provide the required support for the presently claimed genus of inventions.

In view of the uncertainty in the art relating to the effects of protein modifications, and the presence of only a single species of the claimed genus in the application, and the limited guidance in the application as to what specific structures within the N^{pro} sequence should be targeted to achieve the desired function, the disclosure of the application is not deemed to provide sufficient descriptive support to shoe possession of the complete genus as claimed.

17. **(Prior Rejection- Maintained)** Claims 30-34, 36 and 38-41, 46, 47, 54, and 55 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an attenuated BVDV that has about 310 base pairs of the Npro gene intact, does not reasonably provide enablement for the scope of mutations to Npro claimed or an intact Npro. The Applicant traverses the rejection on the grounds that the application need only "supply the novel aspects of an invention in order to constitute adequate enablement," and that as the application indicates the

novel aspect of the invention in the mutation of the N^{pro} and the insertion of the bovine ubiquitin sequence the application has met the enablement requirement. The Applicant additionally asserts that additional inactivating mutations may be identified by routine experimentation, and that they need not specifically point out where such mutations may be made so as to inactive the encoded N^{pro} protein. These arguments are not found persuasive.

With reference to the first argument in traversal, the need to supply only the novel aspects of the invention, it is noted that the court made the statement quoted by Applicant from the decision in *Genentech v. Novo Nordisk* (42 U.S.P.Q. 2d 1001, at 1005, quoted on page 12 of the Response) only to indicate that the specification need not disclose that which was already known in the art. However, this does not absolve an applicant of the need to provide a fully enabling disclosure of the claimed invention. As was also stated in that decision, "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Id. In the present case, the Applicant has not met this burden.

The claims read on a broad scope of possible BVDV variants, including variants comprising any mutation (outside of the 5' 36 base pairs of the N^{pro} gene) that results in the inactivation of the encoded N^{pro} protein. As was indicated in the prior actions, in support of this scope, the Applicant has provided only a single working example of the claimed invention, and has not provided any examples of single base pair modifications that would result in BVDV variants with the require functional characteristics. Moreover, as was also previously indicated, neither the application nor the prior art provide teachings as to what modifications, other than the

deletion of at least the 196 3' base pairs from the N^{pro} gene, would result in the inactivation of the encoded protein.

Thus, the combination of the broad scope of the claims, the limited examples or guidance provided, and the relatively undeveloped state of the prior art (regarding N^{pro} gene structure and function) tend to lead away from a finding of enablement. Even if it is accepted that only routine experimentation would be required to determine if any particular modification did in fact result in a claimed virus (or related claimed product), the fact that the claims are not limited to any particular mutation indicates that this routine screening process is insufficient to demonstrate that the application is enabling for the full scope of inventions claimed.

In addition to the limited guidance or examples presented in the application, in the present case there is an additional factor to be considered. It is accepted in the art that the modification of a protein has unpredictable results in the absence of detailed information on the relationship between the amino acid(s) to be modified and the structure and function of the protein. See e.g., Bowie et al., Science 247:1306-10. This unpredictability in the art, in addition to the other factors =described above and in the prior actions, indicates that the present disclosure is not sufficient to enable those of ordinary skill in the art to make and use BVDV variants in accordance with the full scope of the inventions claimed.

It is additionally noted that the Applicant asserts both that the claims do not encompass an intact N^{pro} protein coding sequence, and that the specification makes it clear that that the region to be mutated is the 3' region of the N^{pro} gene. These assertions are not found persuasive. In particular, this is because the specification on page 7 indicates that the mutations to the N^{pro} sequence may be any substitution, insertion, or deletion that inactivates the N^{pro} protein.

Moreover, while the application indicates that the mutation is in the 3' region, the application also indicates that this region may include the region spanning from the 3' terminus of the N^{pro} gene to anywhere between 194 and 468 base pairs towards to the 5' terminus. See, page 6, lines 30-36 (indicating that the 5' region includes the can encompass at least 36 to about 310 base pairs, indicating that the 3' varies correspondingly). Thus, identifying the 3' region as the region to be mutated does little more than exclude the 5' 36 base pairs, from the 504 base pair sequence, as targets for mutation.

For these reasons, and for the reasons of record, the Applicant's arguments in traversal are not found persuasive, and the rejection is maintained.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. **(Prior Rejection- Maintained)** Claims 30, 33, 36, 38-41, 46, 47, 54 and 55 were rejected under 35 U.S.C. 103(a) as being unpatentable over Behrens et al. (Journal of Virology. 1998; 72 (3): 2364-2372). It is noted that the rejection was previously applied against claims 42 and 44. In view of the withdrawal of these claims from consideration, the rejection is withdrawn from these claims. The Applicant traverses the rejection of the remaining claims on the basis that the reference does not teach embodiments wherein the recombinant virus includes at least 310 base

pairs from the N^{pro} sequence, and does not teach the use of such as an immunogenic composition. These arguments are not found persuasive.

With respect to the first argument, none of the claims require that the claimed virus includes at least 310 base pairs. Each of the rejected claims refers only to the presence of at least 36 base pairs. This limitation is met by reference by the inclusion of 126 base pairs. Pages 2369 (Fig. 5) and 2371 (left column). The Applicant's first argument in traversal is therefore not found persuasive.

It is next noted that claims 30, 33, 36, 38-41 read only on the viruses, the coding vectors, and transfected cells. These claims are silent as to the immunogenicity or other utility of the claimed products. As such, the Applicant's arguments are found unpersuasive with respect to these claims.

With respect to claims 46, 47, 54, and 55, these claims are drawn to immunogenic compositions comprising the viruses and a "veterinarily-acceptable carrier." The application provides no definition as to what constitutes such a carrier. Because there is no such definition, the term is read as including any carrier that could be administered to an animal. The reference teaches the indicated viruses in cell cultures. As there is nothing in the claims to exclude such composition from the claimed compositions, these compositions are deemed to meet the claim limitations. While the Applicant asserts an intended use for such compositions, it is noted that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Because there does not appear to be any structural difference between the

compositions of the reference and those presently claimed, the Applicant's argument regarding the intended use is not found persuasive.

The rejection is therefore maintained for the reasons above, and the reasons of record.

Conclusion

20. Claims 35 and 37 appear allowable over the art.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Z. Lucas 8/9/06
Patent Examiner